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BASIC RESEARCH

PERI-IMPLANTITIS: Uncovering the molecular mechanisms by a Bioinformatics approach

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Abstract

Purpose: update the molecular information in peri-implantitis ; identification and clarification of the most important molecular mechanisms in the establishment and progression of the disease.

Materials and Methods: literature review of peri-implantitis proteome studies (Medline®) ; information collected manually annotated in SalivaTecDB ; functional characterization of peri-implantitis OralOma with bioinformatic strategies. PANTHER® analysis feature to detect statistically enriched molecular functions or biological processes.

Results: increase from 38 to 96 the number of proteins in the SalivaTecDB for this pathology. Increased concentrations of IL-1beta, MPO and TNF-alpha and decreased IL-10 may reflect early stages of peri-implant pathology in which cell recruitment is stimulated. Increase of MMP-8 reflects the onset of peri-implant tissue destruction. Increased RANK, RANKL and decreased OPG are indicators of osteoclastogenesis - essential process for establishment of the disease.

Conclusions: To curb bone resorption intervention must be done at the beginning, before the production of inflammatory mediators.

Background and Aim

Evolution of implantology, associated with socioeconomic reasons, led to an increase in the number of implants placed. This fact, associated to the longer *in vivo* maintenance, has favored the incidence of peri-implantitis. Several publications report an high-rate of peri-implantitis after 10 years, with values around 20%. However, the etiology of this pathology and its mechanisms of action are still not fully understood.

AIM: to update the molecular information in peri-implantitis, through identification and clarification of the most important molecular mechanisms in the establishment and progression of the disease.

Methods and Materials

Literature review Medline®: peri-implantitis proteome studies ; keywords "peri-implantitis", "biomarkers","proteome", "bone diseases" (op: "AND").

Information manually annotated in SalivaTecDB: identification of the protein; source of the sample; up-/downregulation compared to normal samples; sample donor data - age, gender and social habits; methods of sampling and analysis; type of study and whether the protein had been proposed as a biomarker (http://salivatec.viseu.ucp.pt/salivatec-db)

Functional characterization of the OralOma of peri-implantitis: healthy individuals VS with peri-implantitis, using bioinformatic strategies.

PANTHER (http://www.pantherdb.org/) was used to automatically detect statistically enriched molecular functions or biological processes.

Results

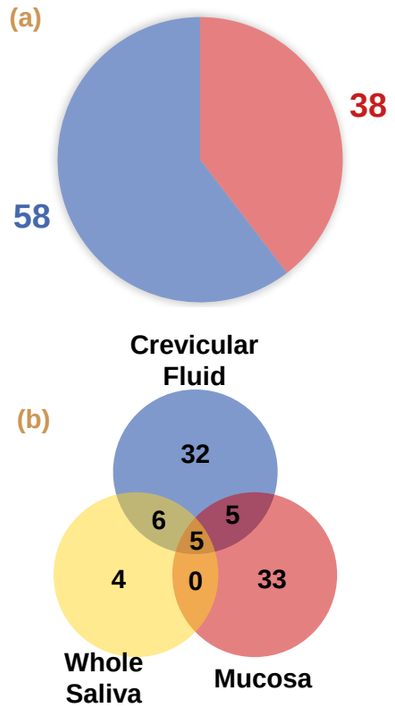

Figure 1 – (a) N.º proteins in this work (blue) compared to n.º proteins previously identified (red) **(b)** Origin of annotated proteins. Data from SalivaTecDB.

- ⇧ 38 to 96: n.º of proteins in SalivaTecDB
- Most of catalogued proteins presented quantification data;
- No homogeneity on units used, methods of collection and analyses;
- Functional analyses: elucidate some common molecular mechanisms between peri-implantitis and periodontitis;
- ⇧ concentrations of IL-1β, MPO and TNF-α and ⇘ in IL-10: early stages of peri-implant pathology - cell recruitment is stimulated;
- ⇧ of MMP-8 reflects the onset of peri-implant tissue destruction;
- ⇧ RANK, RANKL and ⇘ OPG are indicators of osteoclastogenesis: essential process for establishment of disease.

Table 1 – Functional characterization of some of the main proteins identified. Fold change (peri-implantite / control) and potential role in the pathology, in the light of previous knowledge about them are shown.

Protein	Quantification data (Disease / Control)	POTENTIAL ROLE IN PI	Biological function
↑ **TNF-α**	163 | 4,83 | 4 | 3,67	✓ Major mediator in response to Gram - bacteria ([ ] reflects amount of bacteria and stage of inflammation); ✓ Leads to dysregulation of bone metabolism (↑ osteoclasts and ↓ of osteoblasts).	Early stage: Recruitment of cells
↑ **IL-1β**	135,1 | 95,48 | 6,52 46,88 | 7,71	✓ Tissue destruction: • Stimulation of bone resorption; Degradation of ECM.	
↑ **MPO**	14,4 | 4,3	✓ Defense against infectious agents. Under conditions of excessive activation can act against cells of the host; ✓ Decrease after treatment.	
↓ **IL-10**	-5,88 | -2,17	✓ Inhibits the synthesis of proinflammatory cytokines; ✓ Trends to reduce with progression of PI and deepening of the pockets.	
↑ **MMP-8**	9,7	✓ Degradation ECM components and basement membrane (deregulated activity - destruction of peri-implant tissues); ✓ Decrease after treatment.	Production of enzymes for tissue destruction
↑ **RANK**	2,73 | 2,98	✓ RANK / RANKL interaction is required for osteoclasts differentiation. OPG> RANKL → Bone maintenance; RANKL> OPG → Bone resorption.	Osteoclasto--genesis
↑ **RANKL**	23,5 | 1,79		
↓ **OPG**	-3,22 | -2,14 | -1,47		

Conclusion

- Although other studies suggest OPG as an option to curb bone resorption this would be a short-term solution, since the intervention would occur at the end of the process - not reversing the disease.
- Intervention must be done at the beginning of the process, before the production of inflammatory mediators.
- **Propose: the modelling of immune cells should be studied in future works in order to identify the best therapeutic targets.**

References

1. Zani SR, Moss K, Shibli JA, Teixeira ER et al. Peri-implant crevicular fluid biomarkers as discriminants of peri-implant health and disease. Journal of Clinical Periodontology. 2016 Oct;43(10):825–832;
2. Rakic M, Struillou X, Petkovic-Curcin A, Matic S, Sanz M, et al. Estimation of bone loss biomarkers as a diagnostic tool for peri-implantitis. Journal of Periodontology. 2014 Nov;85(11):1566–1574;
3. Carcuac O, Berglundh T. Composition of human peri-implantitis and periodontitis lesions. Journal of Dental Research. 2014 Nov;93(11):1083–1088;

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